Prevention of Infections Associated With Combat-Related Burn Injuries

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Abstract: Burns are a very real component of combat-related injuries, and infections are the leading cause of mortality in burn casualties. The prevention of infection in the burn casualty transitioning from the battlefield to definitive care provided at the burn center is critical in reducing overall morbidity and mortality. This review highlights evidence-based medicine recommendations using military and civilian data to provide the most comprehensive, up-to-date management strategies for initial care of burned combat casualties. Areas of emphasis include antimicrobial prophylaxis, debridement of devitalized tissue, topical antimicrobial therapy, and optimal time to wound coverage. This evidence-based medicine review was produced to support the *Guidelines for the Prevention of Infections Associated With Combat-Related Injuries: 2011 Update* contained in this supplement of *Journal of Trauma*.

Key Words: Burns, Thermal injury, Military, Combat, Infection.

(*J Trauma.* 2011;71: S282–S289)

Thermal injury is common to all modern military conflicts.[1] As a result of explosive devices being used against military personnel involved in Operation Iraqi Freedom and Operation Enduring Freedom, burns were identified as the primary cause of injury in ~5% of military personnel evacuated from these battlefields.[2] The concept of the dedicated burn unit is a product of wartime and disaster experience and is closely tied to developments in infectious disease treatment. Archibald McIndoe, civilian consultant to the Royal Air Force in plastic surgery, established a burn ward at the East Grinstead hospital in 1940. The focus of his work was postburn reconstruction.[3] After the Cocoanut Grove nightclub fire in Boston in 1942, Cope et al. established a temporary ward at the Massachusetts General Hospital dedicated exclusively to the care of the surviving burn patients. The results of the Cocoanut Grove experience were carefully documented in a monograph with the chapter on infections written by Dr. Champ Lyons, a surgeon and microbiologist.[4] Lyons later became the director of the Wound Unit at Halloran General Hospital, Staten Island, NY, the forerunner of the US Army Surgical Research Unit.[5] The initial focus of the unit was to characterize the role of newly discovered antibiotics in the treatment of war wounds.[6] The Surgical Research Unit moved to Fort Sam Houston, TX, in 1947, and the US Army Burn Center was established there in 1949, in response to the growing threat of nuclear war and concern that the large number of burn injuries that resulted from the bombing of Hiroshima would characterize future conflicts.[7] Once established, the US Army Burn Center focused research efforts on improving postburn resuscitation and preventing renal failure and burn wound sepsis.[7] The research in these areas has continued to evolve with ensuing military conflicts.

The evacuation of burned personnel has also evolved with each new conflict to which the US military has responded. During the Vietnam War, burned personnel were evacuated to an US Army general hospital in Japan, where they were treated for variable periods (days to weeks) before transfer to the United States.[1,8,9] During the operations in Iraq and Afghanistan, thermally injured US military personnel have arrived in the continental US (CONUS) for definitive care ~4 days after injury.[10] During the course of an evacuation from Iraq or Afghanistan, patients transition through several medical facilities with differing levels of capabilities before arriving at a major US medical center.

The US military currently uses a role-based treatment and evacuation in which injured personnel initially receive basic resuscitation and hemorrhage control by embedded military medics (Role 1). Some patients undergo initial medical therapy at facilities staffed by physicians or physician assistants (Role 2a). Casualties who require further care are transported to a facility that can provide initial surgical intervention, such as a forward surgical team (Role 2b), or more often a combat support hospital (Role 3) that contains surgical subspecialists and intensive care capabilities. Personnel who require ongoing care are transported to Landstuhl Regional Medical Center in Germany (Role 4) and from

Submitted for publication April 22, 2011.
Accepted for publication June 3, 2011.

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Supported by the US Army Medical Command for the consensus conference and publication of the *Journal of Trauma* supplement.

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DOI: 10.1097/TA.0b013e318227adc2

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 AUG 2011	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Prevention of infections associated with combat-related burn injuries	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
D'Avignon L. C., Chung K. K., Saffle J. R., Renz E. M., Cancio L. C.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**8**	

there, burn casualties are transported to the US Army Institute of Surgical Research (USAISR), the US Army Burn Center at Fort Sam Houston, TX (Role 5). The method of transport varies with the severity of injury. The most critically injured patients are transported by the USAISR Army Burn Flight Team or US Air Force Critical Care Air Transport Teams. Burn casualties with less severe burns and ambulatory patients with minimal injuries may be transported on scheduled evacuation flights supported by US Air Force Aeromedical Evacuation teams.[11] The criteria for evacuation of burn patients from theater based on burn severity are listed in Table 1. Evacuation to the USAISR is recommended for casualties with moderate or severe burns or any burns involving the hands, face, or perineum. In addition to surgical and nursing expertise, the USAISR provides the intensive rehabilitation and psychologic support necessary for these patients throughout the recovery process, as well as future reconstructive surgery.

Historically, burn wound infection was the most common cause of death in the thermally injured patient. Fortunately, advances in care have led to a decline in the occurrence of burn wound infection. However, wound infection remains a concern, particularly in the setting of delays in definitive surgical care, such as may occur in the combat environment. A recent autopsy study of 74 burns patients treated at the USAISR Burn Center found infection of wounds or the lower respiratory tract were the causes of death in 61% of patients.[12] The 36 patients who sustained burn injuries as a result of combat operations in Iraq and Afghanistan were more likely to die from infection (75%) than the 38 patients who sustained noncombat-related burns (47%). The potential explanations for this finding are myriad but include differences in time to definitive care, differences in total body surface area (TBSA) burned, and differences in rates of inhalational injury between combat and noncombat burns. The clinical picture is further complicated by the fact that combat-associated burn casualties often suffer concomitant traumatic injuries. An evaluation of 540 combat-related burn casualties found that 50.9% had multiple traumatic injuries.[11] The best method of caring for thermally injured casualties, including those with multiple, concomitant traumatic injuries as they transition from the battlefield setting has yet to be determined. However, the importance of infection as a cause of mortality in this patient population cannot be overemphasized; therefore, the prevention of infections in the burn patient as he or she transitions from the battlefield to definitive care at USAISR is the focus of this review.

METHODS

A MEDLINE search was performed on December 15, 2010, and January 20, 2011, using the key words "burns," "thermal injury," "military," "combat," "infection," "prevention," and "wound infection."

MICROBIOLOGY AND EPIDEMIOLOGY OF BURN WOUND INFECTION

The microbial epidemiology of burn wound infections has evolved during the past 20 years as use of topical antimicrobials, routine wound care, early burn wound excision, and definitive coverage with autograft have become standard practices. Evidence suggests that the incidence of bacterial burn wound infection has declined, first because of effective topical antimicrobials and second because of the practice of early excision and grafting (although data on this latter practice are inconclusive in the setting of large burns).[13–17] A meta-analysis of all available randomized controlled studies found a reduction in mortality with early excision for all burn patients without inhalation injuries.[17] Early excision and grafting has become standard practice in most US burn centers. Early excision and grafting, before arrival at the USAISR Burn Center, is not currently practiced because it would further expose the patient's open wounds to the environment as they transit multiple facilities, across thousands of miles, enroute to definitive care.[11] Knowledge of pre-excision burn wound flora is important to understanding the risks for burn wound infection in military personnel.

Most of the available data on the bacteriology of burn wound infections have been taken from studies performed before the practice of early excision and grafting. Although the incidence of infection has decreased as a result of early excision and grafting, the list of offending microorganisms

TABLE 1. Recommendations for the Evacuation of Burn Patient From the Combat Zone[10]

Category	Burn Severity*	Evacuation Recommendation
1	Limited partial-thickness burns not involving hands, joint, face, and perineum	Air evacuation to Landstuhl for wound care with expected return to duty
2	Limited partial-thickness burns involving hands, joint, face, and perineum, or any limited full-thickness burn	Air evacuation to US Army Institute of Surgical Research (USAISR) Burn Center
3	Moderate partial- or full-thickness burns, patient stable	Transfer to USAISR Burn Center via Critical Care Air Transport Team (CCATT)
4	Severe partial- or full-thickness burns and/or inhalation injury requiring intubation, patient stable	Transfer to USAISR Burn Center via Burn Flight Team (Special Medical Augmentation Response Team, SMART-Burn)
5	Severe partial- or full-thickness burns, patient unstable for air evacuation to United States	Transfer to a European burn center
6	Vesicant casualties	Air evacuation to USAISR Burn Center

* Burn severity definitions: limited, <10% TBSA; moderate, 10% to 30% TBSA; severe, >30% TBSA.

responsible for infection has not changed significantly.[12,18–22] In the absence of topical antimicrobials, the immediate postburn period is characterized by rapid colonization of the injured tissue by resident microbial flora.[19–22] Gram-positive skin flora such as *Streptococcus pyogenes* and *Staphylococcus aureus* reside deep within skin appendages and colonize the wound within the first 24 hours to 48 hours after injury.[19,20] Endogenous gram-negative bacteria from the patients' gastrointestinal tracts, such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Escherichia coli*, colonize the wound within the first 48 hours to 72 hours after injury.[19,20] Microorganisms may also be transferred to the burn wound from contaminated surfaces, equipment, or the hands of health care workers.[23–27] Of the many bacterial microorganisms that colonize the burn wound surface after injury, *S. aureus*, *P. aeruginosa*, and *K. pneumoniae* are the most likely to result in an invasive infection.[12,18,21,27,28] This finding is in part a result of the array of virulence factors possessed by these organisms. An autopsy study of patients with burns sustained in combat operations in Iraq and Afghanistan identified *P. aeruginosa* and *K. pneumoniae* as the microorganisms most frequently associated with mortality.[12] A retrospective study performed on patients with combat-related burns admitted to the USAISR Burn Unit found *K. pneumonia* bacteremia to have a higher associated mortality then bacteremia caused by *P. aeruginosa* or *S. aureus*.[28] The increased mortality associated with *K. pneumoniae* bacteremia was independent of age and TBSA, which are the characteristics that historically have had the greatest impact on mortality for patients with burns. The mortality associated with this pathogen, coupled with dwindling antibiotic treatment options because of increasing rates of extended-spectrum β-lactamase production, highlight the importance of preventing invasive infection.

In addition to these pathogens, the US military health care system has experienced an increased rate of multidrug-resistant *Acinetobacter calcoaceticus-baumannii* (Acb) complex infections in military personnel injured in Iraq and Afghanistan. The UK military has also experienced an increase in Acb infections. A study performed in the United Kingdom by Miranda et al.[29] evaluated the microorganisms involved in wound colonization and infection in both plastic surgery and burn patients. The authors found that military patients with combat-associated injuries were more likely to have wound colonization or infection with *S. aureus*, Acb, and *P. aeruginosa* than civilians treated in the same center. However, the impact of Acb infections remains uncertain. A retrospective cohort study by Albrecht et al.[30] found that although multidrug-resistant Acb is a frequent cause of infection in burn patients, it did not independently affect mortality in this population.

Burn patients are also subject to tetanus if inadequately immunized. A minor burn wound has been associated with fatal tetanus in at least one case report.[31] Therefore, we strongly recommend that the tetanus immunization status of all burn patients be determined. Clinicians should administer tetanus immunization to patients whose last booster was given more than 5 years ago and tetanus vaccination plus antitetanus immunoglobulin should be administered to patients who have no history of vaccination. Booster vaccination should be administered at 4 weeks and 6 months for this latter group.

Yeasts (e.g., *Candida* spp.) and filamentous fungi (e.g., *Aspergillus* spp.) are of increasing importance as a cause of invasive burn wound infection since the introduction of topical antimicrobial agents that have diminished the impact of bacterial infection.[18,22] Candidal colonization of burn wounds is more common than invasive disease and may arise from an endogenous or exogenous source.[31–33] The filamentous fungi are uniformly acquired from an exogenous environmental source and are much more likely to cause invasive disease than *Candida* species.[32–36] The filamentous fungi commonly associated with burn wound sepsis include *Aspergillus* spp., *Fusarium* spp., and members of the Mucorales order of the Zygomycetes.[37] An autopsy study of patients with burns sustained in combat operations in Iraq and Afghanistan found organisms with *Aspergillus*-like morphology or *Mucor*-like morphologies to be the leading cause of mortality as a result of fungal infections.[12] In addition, these organisms were the next most common cause of infection-related mortality after *P. aeruginosa* and *K. pneumoniae*. There have also been case reports of invasive wound infection caused by a variety of dematiaceous fungi such as *Curvularia* spp.[38] Infections caused by filamentous and dematiaceous fungi are clinically challenging as they prove difficult to diagnose in the absence of a biopsy with interpretation by a skilled pathologist. A recent retrospective analysis of patients with thermal burns admitted to the USAISR Burn Center found that fungal burn wound infection is an independent predictor of mortality in patients with TBSA of 30% to 60%.[33] Fungal pathogens typically become a concern later in the treatment course after patients have undergone operation and received broad spectrum antibacterials and should not be a frequent cause of infection in the first few days after injury.[22,32]

Viral infections of burn wounds are rarely reported but do occur. Members of the herpes virus family, including herpes simplex virus and varicella zoster virus, are the most common culprits.[36,39] Cutaneous disease typically occurs in healing partial thickness burns and donor sites.[39] Cutaneous infection follows a benign course if recognized and treated early with topical therapy. Fortunately, invasive disseminated herpes simplex virus or varicella zoster virus is a rare occurrence in the burn patient but should be considered in the patient with cutaneous disease, concomitant pneumonitis, hepatitis, or meningitis as these patients will require systemic therapy.[36,39]

SYSTEMIC PREDEBRIDEMENT ANTIBIOTIC PROPHYLAXIS

The use of prophylactic systemic antibiotics is now well accepted in a wide variety of settings, including the combat casualty who presents with traumatic injuries. However, for the treatment of burns, use of systemic antibiotics for prophylaxis of subsequent burn wound infection has not been proven effective, either routinely (e.g., on admission) or at the time of wound debridement. Note that debridement

refers to the practice of removing devitalized tissue and debris in conjunction with routine wound care and dressing changes and should be distinguished from the surgical excision of the eschar. The early use of antibiotics such as penicillin or erythromycin (aimed at controlling *Streptococcus* outbreaks) has been anecdotally observed to be associated with an increase in infections caused by resistant *Staphylococcus*,[40] although this is not a uniform finding.[41] No study has demonstrated a reduction in burn wound infections with the use of prophylactic antibiotics, and at least one study has shown an increased incidence of infections from Gram negatives, including *Pseudomonas*.[42] The only exception to this finding might be the use of antibiotic prophylaxis against staphylococcal toxic shock (STS), which can be a problem in pediatric burn care.[43] However, the use of prophylactic antibiotics for prevention of STS in children remains controversial. Routine systemic antimicrobial prophylaxis is not recommended for the burned patient undergoing rapid evacuation for definitive care. There are insufficient data to recommend for or against its use in patients with concomitant inhalation injury, and insufficient data to recommend for or against its use in children. In the event that a burn patient suffers from concomitant traumatic penetrating injury or fracture, antibiotic prophylaxis should be administered in accordance with the updated clinical practice guidelines published in this *Journal of Trauma* supplement.

SYSTEMIC PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS

Antibiotic prophylaxis has also been examined in burn surgery. Few studies have supported the use of systemic antibiotic prophylaxis during excision and grafting procedures. In particular, antibiotics appear to be of no value in the prophylaxis of wound infections accompanying surgery for small burns.[44] The role of perioperative prophylaxis for excision and grafting of large burns (>40% TBSA) has not been well studied. Early studies documented a significant incidence of transient bacteremia associated with wound manipulation,[45] but a more recent evaluation showed this incidence to be much reduced.[46] Antibiotic administration has been found to reduce the incidence of this transient bacteremia but not to affect outcomes.[47] A recently published study by Ramos et al.[48] found that the use of systemic antibiotics administered perioperatively to patients undergoing grafting of deep burns was associated with improved autograft survival. However, the study had several limitations, including a small sample size, and more extensive follow-up studies will be required. Because of the limited evidence, controversy on this topic exists; and burn units vary widely in their practices of providing perioperative antibiotic prophylaxis.[49,50] Although the data are inconclusive, the clinician may consider the use of perioperative systemic antibiotics for excision and grafting procedures. The ideal regimen will vary based on the local antibiotic resistance patterns. The current practice at the USAISR Burn Center is to provide 24 hours of perioperative antibiotic prophylaxis with vancomycin and amikacin.

It is crucial to note that systemic antibiotic therapy is clearly indicated in the surgical treatment of infected burn wounds. Empiric treatment of patients with large open wounds and evidence of infection may be necessary. Many patients with large burns develop symptoms such as fever and leukocytosis as a consequence of the systemic response to injury, rather than infection, further complicating decisions regarding the use of antibiotics.[51] Thus, diagnosis of burn wound infection requires close attention to the patient's overall clinical status and to daily inspection of the appearance of the wound, as described elsewhere.[52] Examination of full-thickness wound biopsies by a qualified pathologist is the definitive diagnostic procedure.[52]

TOPICAL ANTIMICROBIAL USE

In contrast to the uncertainty regarding the use of systemic antibiotic prophylaxis for burns, the use of topical antimicrobials, in conjunction with aggressive wound care and early excision and grafting, has been associated with a significant decline in the incidence of burn wound infections.[17,52–54] Topical antimicrobials and aggressive wound care should be performed at the lowest role possible and should be continued as the patient moves through the subsequent roles of care. Aggressive debridement of debris and devitalized tissue may not be feasible at lower roles. In this situation, clean, dry dressings should be applied to burn wounds and topical antimicrobials may be withheld until the patient is transferred to a higher level of care. There are limited data on how soon after injury debridement and application of topical antimicrobials should be performed; the opinion of the authors is that this should be performed within 8 hours of injury, assuming concomitant traumatic injuries have been adequately addressed.

Management recommendations based on burn severity are summarized in Table 2. First-degree and superficial partial-thickness burns may be treated with topical antimicrobials and daily dressing changes alone.[52–54] The use of temporary biosynthetic materials such as Biobrane (UDL Laboratories, Rockford, IL) is also an option for superficial partial-thickness burns. There are no data related to use of Biobrane in a field or combat environment. However, it is strongly recommended that Biobrane be considered only for patients with clean, fresh burns, which are rarely encountered in the deployed environment.[55–57] We recommend that deep partial-thickness and full-thickness burns be treated with topical

TABLE 2. Management of Burn Wounds Based on Depth[16,17,20,52–55,58,59]

Wound	Interventions
First degree	Symptomatic care
Superficial partial thickness	Topical antibiotics with twice-daily dressing change, silver-impregnated dressing changed every 3–5 d, or Biobrane*
Deep partial thickness	Topical antibiotics with twice-daily dressing change, or silver-impregnated dressing changed every 3–5 d and excision and grafting
Full thickness	Topical antibiotics with twice-daily dressing change and excision and grafting

* Recommend restriction to individuals experienced with its use.

antimicrobials with twice daily dressing changes, followed by early excision and grafting at the burn center.[13–17,52–54] If definitive surgical care must be accomplished in theater, such as when evacuation of host nation patients is not possible, we recommend that the procedure be performed only at a role 3 facility to offer the benefits of staffing, supplies, and equipment related to this level of care.

The importance of wound care—both at the time of initial debridement and at each dressing change thereafter—cannot be overemphasized. Wound care should be directed at thoroughly removing devitalized tissue, debris, and previously placed antimicrobials. A broad-spectrum surgical detergent such as chlorhexidine gluconate should be used for cleansing wounds during dressing changes. Adequate analgesia (e.g., frequent small doses of intravenous narcotics or ketamine), along with preemptive anxiolysis (e.g., preprocedure oral benzodiazepine), is necessary to permit adequate wound care. The most commonly used topical antimicrobials for the prevention and treatment of burn wound infection are mafenide acetate, silver sulfadiazine, silver nitrate solution, and silver-impregnated dressings.[52–54,58] Mafenide acetate and silver sulfadiazine are the topical agents typically available in the deployed environment. A brief review of each of these agents follows.

Mafenide Acetate

Mafenide acetate (Sulfamylon) was first introduced to burn care in 1964.[52] A retrospective study comparing USAISR Burn Center patients treated in the pre-mafenide era (1962–1963) with those treated after the introduction of mafenide found a decrease in overall burn mortality from 38% to 20% and a reduction in the rate of invasive burn wound infection from 22% of admissions to 2%.[52]

Mafenide acetate is available as an 11% water-soluble cream composed of α-amino-p-toluenesulfonamide monoacetate. Despite the name, it is functionally a nonsulfonamide antibiotic. It rapidly penetrates full-thickness eschar and exerts a broad antibacterial effect.[59] In vitro and animal studies have demonstrated mafenide acetate to have efficacy against *Staphylococcus* and *Pseudomonas* species.[60,61] Although resistant strains of *Providencia* and *Enterobacter* developed at the USAISR in the late 1960s, none of the nearly 8,500 strains of *P. aeruginosa* isolated from USAISR burn patients during the period from 1967 to 1992 were resistant to clinically relevant concentrations of the drug.[62] There are some drawbacks to the use of mafenide acetate. It has no efficacy against filamentous fungi and induces pain on application, a consequence of its otherwise desirable ability to penetrate eschar and reach viable tissue. The drug and its primary metabolite (p-carboxybenzenesulfonamide) are inhibitors of carbonic anhydrase, and metabolic acidosis has been reported in patients with extensive burns treated twice daily.[63] Patients with inhalation injury are at greater risk for metabolic acidosis if their pulmonary dysfunction limits respiratory compensation.[63] This may pose a problem given that concentrations of the drug in eschar drop below therapeutic levels approximately 10 hours after application, necessitating twice-daily dosing unless a second agent is also used.[59] One common practice at the USAISR Burn Center is to apply mafenide acetate in the morning and silver sulfadiazine 12 hours later to realize the benefits of both drugs while limiting their toxicities.[62]

Mafenide acetate is also available in powder form for reconstitution as a 5% aqueous solution. This solution is used to moisten gauze dressings and is indicated for topical treatment of wounds after skin grafting. In addition, we often use this solution, along with twice-daily gauze dressing changes, for the topical treatment of deep partial-thickness burns of limited extent. However, this formulation has been shown to be less effective than mafenide acetate cream in preventing death in a murine model of *Pseudomonas* burn wound infection.[64]

Silver Sulfadiazine

Silver sulfadiazine (Silvadene, Thermazine, Flamazine, SSD, Burnazine) is available as a 1% water-soluble cream. It was developed in 1968 by complexing silver nitrate and sulfadiazine.[61,65] Previously, sulfadiazine alone had been used as a topical agent, but the development of resistance became an issue. Complexing sulfadiazine with silver nitrate has largely overcome the resistance problem, and the agents appear to act synergistically. In essence, the complex acts as a slow-release formulation of silver cation.[66,67] Much like mafenide acetate, silver sulfadiazine exhibits activity against gram-negative and gram-positive organisms; however, unlike mafenide, it has poor eschar penetration.[61,66,67] The advantages of silver sulfadiazine are that it is relatively painless on application and that it has some activity against *Candida* species (but not against filamentous fungi). Rarely, a decrease in the neutrophil count has been observed with initiation of therapy, attributed to depression of granulocyte macrophage progenitor cells in the marrow.[65] This effect typically resolves even when the agent is continued and rarely necessitates discontinuation of therapy.[65]

Silver Nitrate Solution

Silver nitrate ($AgNO_3$) solution was first introduced in 1964 as topical prophylaxis against burn wound infection. It had been previously used as a 10% solution that was found toxic to tissue.[67] It is now used as a 0.5% aqueous solution, a concentration which is not toxic to regenerating epithelium.[58,67] Burn wounds are dressed with multiple thick layers of coarse mesh gauze to which the silver nitrate solution is frequently reapplied to keep the gauze continuously moist.[62] Much like silver sulfadiazine, it exhibits activity against gram-positive bacteria, gram-negative bacteria, and *Candida* spp. The major drawbacks to silver nitrate solution are that it has poor penetration of eschar, requires the use of occlusive dressings, and turns black on contact with tissues.[67] Dressings must be changed twice daily to prevent buildup of exudate or of tissue-toxic levels of the silver nitrate. The need for continuously moist dressings means that patients with large wounds are at risk of hypothermia, particularly during transport or in general hospital rooms. Another drawback to this drug is the depletion of cations caused by leeching across the open wound into the hypotonic solution. This phenomenon may result in hyponatremia, hypocalcemia, hypokalemia, and hypomagnesemia; therefore, close monitoring of electrolytes is necessary.[58]

Silver-Impregnated Dressings

A variety of dressings impregnated with elemental silver have been approved by the US Food and Drug Administration (FDA) as topical therapy for burns. Several varieties of these dressings are now available, but their equivalency in silver delivery and antimicrobial efficacy is difficult to assess. Some examples of available silver dressings include Silverlon (Argentum LLC, Willowbrook, IL), SilverSeal (Noble Biomaterials, Scarnton, PA), and Acticoat (Smith and Nephew, Hull, United Kingdom). Silverlon is a knitted fabric composed of pure nylon-based fibers, covered uniformly and circumferentially with a thin coat of metallic silver. Alone and in combination with weak direct current, silver nylon has been shown to be effective in a lethal *Pseudomonas* murine model.[68] Acticoat is a rayon or polyester core encased in a dense polyethylene mesh coated with nanocrystalline silver. Tredget et al.[69] have reported Acticoat to be more effective than silver nitrate solution with respect to preventing heavy burn wound colonization (10^5 organisms per gram of tissue). Silverlon, SilverSeal, and Acticoat are approved for use in superficial and partial-thickness burns and can be left in place for several days thereby lessening the burden related to dressing changes. Clinicians should consider use of these agents for the treatment of wounds sufficiently small that outpatient or ward care are reasonable options.[70] The method of application for each of the topical agents is summarized in Table 3.

Excision and Grafting

Early excision of burned tissue and coverage with skin grafts or skin substitutes has been associated with a decrease in mortality among patients without concomitant inhalation injury.[16,17,20] The beneficial effect of this practice on mortality is likely multifactorial, with a decreased incidence of wound infection[18] and with the removal of devitalized tissue (which otherwise would prolong the inflammatory process) both playing a role. The definition of "early" excision has not been definitively established. Studies have variably defined early excision as that performed either at admission or up to 5 days after injury.[16,17,20] Early excision and grafting for deep partial-thickness and full thickness burns is recommended as soon as it is practical to do so. The accurate assessment of burn depth is challenging, and it is often difficult to predict the ultimate fate of a burn within hours to days of injury. In fact, some burns may progress from partial to full thickness during a period of days; thus, careful daily examination is critical.[74]

If excision is performed, the entire burn wound may be excised in a single procedure or in serial procedures performed during the course of several days.[55] Definitive coverage requires the application and successful integration of autograft. If sufficient autograft is not available, options for temporary wound coverage after excision include biological and synthetic coverings. Temporary biological dressings consist of allografts and xenografts. Allografts may be used to protect an excised wound or as an overlay to protect an excised wound after application of widely meshed (e.g., 3:1, 4:1) autograft. Fresh allograft may be available in the United States, but more often is frozen. A shelf-stable allograft product, GammaGraft, has been used in the combat zone during Operation Iraqi Freedom.[10] Xenografts (such as pig skin) are typically used as temporary coverage of wounds expected to heal.[74] Temporary synthetic skin substitutes are available. Biobrane is an example of a synthetic covering that is appropriate for clean partial-thickness burns. This, and similar products, act as a wound barrier and prevent evaporative losses but have no intrinsic antimicrobial properties.[55] Integra, a bilaminar product (inner dermal analog of chrondoitin-6-sulfate and collagen; outer temporary epidermal analog of silicone) should only be used by surgeons experienced in its use and under optimal conditions such as those available in a burn center.

As previously noted, surgical excision is normally not performed in the combat zone because it is labor- and supply-intensive and because optimal outcomes require the multidisciplinary capabilities present only in a burn center. However, definitive surgical care for local nationals may be required in the combat zone. We recommend that it be performed by qualified individuals at Role 3 facilities,[75] recognizing that this situation is far from ideal.

RESEARCH GAPS

Many gaps exist in our knowledge of the best methods of preventing and/or treating burn wound infections. As noted previously, a number of new dressing products which contain silver or (potentially) other antimicrobials have the potential to greatly facilitate wound care by permitting application earlier in the course of therapy, and by requiring far less frequent dressing changes with less pain, cost, and utilization of personnel. However, the ability of these agents to prevent infection in eschar-covered wounds appears to be limited but has not been studied adequately. The role of these topical agents in treating established wound infections is also not clear.

TABLE 3. Topical Antimicrobial Agents[41,58–63,65–67,71–73]

Agent	Application	Penetration	Side Effects
Mafenide acetate cream	Apply 1/16 inch layer twice daily*	Penetrates eschar	Painful on application, metabolic acidosis
Silver sulfadiazine cream	Apply 1/16 inch layer twice daily*	Poor eschar penetration	Transient leucopenia
Silver nitrate solution	Dress wounds with multiple layers of coarse gauze and apply solution to keep gauze continually moist	Poor eschar penetration	Electrolyte disorders
Acticoat, Silverlon, or Silverseal†	Moisten dressing with sterile water, cut to size, secure to wound with secondary dressing, change in 3–5 d	Poor eschar penetration	

* Consider alternating mafenide in the morning with silver sulfadiazine in the evening.
† Application information obtained from package insert.

CONCLUSIONS

The occurrence of invasive burn wound infection has decreased with the widespread use of topical antimicrobials, early excision and grafting, and the implementation of strict infection control measures in most centers. However, the uniquely austere environment encountered in the combat zone raises the issue of how best to prevent infection in injured military personnel. Wound care and the use of prophylactic topical antimicrobials should occur as soon as possible in the evacuation process. The use of systemic antimicrobials should be avoided during the evacuation process to minimize selective pressure for resistant organisms. Perioperative prophylaxis with systemic antimicrobials can be considered for excision and grafting procedures. The recommendations offered by this article will certainly evolve, along with our knowledge of the unique risks posed to the burn patient receiving initial care in the combat environment.

ACKNOWLEDGMENTS

We thank Ms. Otilia Sánchez for editing the manuscript.

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